Please amend the Abstract as follows:

ABSTRACT OF THE DISCLOSURE

The preparation of macrocyclic molecules from linear, synthetic thioester precursors is disclosed. An excised thioesterase domain isolated from either a polyketide synthases (PKS) or non-ribosomal peptide synthetases (NRPS) multidomain system catalyzes the cyclization reaction. Thioester substrates also are described that are efficiently cyclized by the method of the present invention. Additionally, macrocyclic molecules, including macrolactones and macrolactams, that are prepared by the macrocyclization methods of the invention are described.

Please amend the paragraph beginning at line 8 on page 45, as follows:

A systematic representation of the successive pentapeptide dimerization and decapeptide cyclization reactions catalyzed by the TE domain from Gramicidin S synthetase in the natural context of the intact NRPS protein (GrsB) is depicted in FIG. 3(b) and Gramicidin S synthetase from *B. Brevis* is illustrated in FIG. 3(a). The sequence of steps in the reaction are (i) a pentapeptide is built up by the ~~syntetase~~ synthetase and transferred to the TE active site serine, (ii) a second pentapeptide is ~~uilt~~ built up, (iii) the N-terminal amine of the pentapeptide-S-PCP reacts with the peptide-O-TE to form a decapeptide-S-PCP intermediate, and (iv) the PCP-tethered decapeptide is transferred to the TE serine and cyclized. A systematic representation of an illustrative example of the elongation/cyclization method of the invention is depicted in FIG 3(c) where a pentapeptide thioester (GLP 5) undergoes dimerization and successive macrocyclization of the resulting decapeptide thioester catalyzed by the excised TE domain protein from the tyrocidine NRPS (TycC TE) to form the cyclic peptide antibiotic gramicidin S. A HPLC analysis of this reaction after one (1) minute is presented in FIG 3(d) where the reaction initially contained 200 μM GLP5, 100 nM TycC TE and 25 mM MOPS (pH 7.0, 24 °C).

Please amend the paragraph beginning at line 16 on page 46, as follows:

The macrocyclization method of the invention is also capable of cyclizing peptide-thioester substrates wherein one or more of the amide linkages between residues has been replaced with ester linkages. Preferred depsipeptide-thioester substrates include those abovementioned in Formula (VII) wherein one or more occurrence of X is an O atom. A non-limiting example of such a substrate is compound 22, an analog of Example 3, wherein there is an ester linkage between residues Phe3 and D-Phe4, and compound 23, an analog of Example 3, wherein there is an ester linkage between residues Tyr7 and Val8. Cyclization rates for TE domain catalyzed macrocyclization of compounds 22 and 23 are similar to the rate observed for the substrate in Example 3 which has the wild-type tyrocidine A sequence (data not shown). Other preferred substrates include those abovementioned in Formula (VII) where Nuc is a hydroxyl group (Nuc = OH). A non-limiting example of such a substrate is compound 24, an analog of Example 3. Compound 24 is macrocyclized by the excised TE domain protein from tyrocidine synthetase (data not shown).

Please amend the paragraph beginning at line 1 on page 47, as follows:

In other specific embodiments of the invention, one or more substrate non-recognition element amino acid residues can be replaced with a non-peptidic linker or a non-peptidic linker can be inserted into a specific point in a chosen peptide sequence such that these substrates remain viable for the TE domain catalyzed cyclization method of the present invention. Substrates comprising a non-peptidic linker have sufficient amino acid residues and main-chain linker atoms to generate a macrocyclic molecule with at least 15 atoms in the macrocyclic ring. In non-limiting examples, 3 or 6 residues of the wild-type peptide-thioester substrate for the excised TE domain from tyrocidine synthetase (Example 3) were replaced with O-(2-(2-aminoethoxy)ethyl)glycolate (25) or the dimer thereof (26). Substrates 25 and 26 are cyclized by the TE domain from tyrocidine synthetase to form 30-member macrocyclic compounds (Data not shown).